K123320

510k Summary

FEB 15 2013

Dimension® Ammonia Flex® reagent cartridge (AMM)

This summary of 510(k) safety and effectiveness information is submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

1. 510(k) Number

2. Applicant: Rose T. Marinelli
Siemens Healthcare Diagnostics, Inc.
P.O. Box 6101, Newark, DE 19714-6101
Office Number: 302-631-8805; Fax Number: 302-631-6299

3. Date: October 25, 2012

4. Proprietary and Established Names:

Dimension® Ammonia Flex® reagent cartridge, (AMM)

5. Regulatory Information:

Ammonia (AMM) Flex® reagent cartridge

Regulation section: 21 CFR 862.1065 Enzymatic Method, Ammonia
Classification: Class I
Product Code: JIF
Panel: Clinical Chemistry

6. Predicate Devices:

The predicate device used to demonstrate substantial equivalence to the Dimension® Ammonia (AMM) Flex® reagent cartridge is the Dimension® Ammonia (AMON) previously cleared under k863840.

7. Device Description:

The Dimension® Ammonia assay (AMM) is an enzymatic method that uses glutamate dehydrogenase (GLDH) and a stabilized NADPH analog. Ammonia reacts with α-ketoglutarate and reduced cofactor to form L-glutamate and the cofactor. The reaction is catalyzed by glutamate dehydrogenase. The decrease in absorbance due to the oxidation of the reduced cofactor is monitored at 340/700 nm and is proportional to the ammonia concentration.

$$\alpha\text{-ketoglutarate} + NH_4^+ + \text{reduced cofactor} \xrightarrow{GLDH} \text{L-glutamate} + \text{cofactor} + H_2O$$

8. Intended Use:

The AMM method is an *in vitro* diagnostic test for the quantitative measurement of ammonia in human plasma (heparin or EDTA) on the Dimension® clinical chemistry system. Ammonia

measurements are used in the diagnosis and treatment of severe liver disorders such as cirrhosis, hepatitis and Reye's syndrome.

9. Indication(s) for Use:

The AMM method is an *in vitro* diagnostic test for the quantitative measurement of ammonia in human plasma (heparin or EDTA) on the Dimension® clinical chemistry system. Ammonia measurements are used in the diagnosis and treatment of severe liver disorders such as cirrhosis, hepatitis and Reye's syndrome.

10. Substantial Equivalence Information:

Both the Dimension® Ammonia Flex® reagent cartridge (AMM) assay and the predicate Dimension® Ammonia Flex® reagent cartridge (AMON) assay employ prepackaged reagents for use on automated clinical chemistry test systems. A comparison of the similarities and differences between the devices is provided in the following tables:

Similarities for Dimension® AMM assay:

Feature	**New Device : Dimension® Ammonia Flex® reagent cartridge (AMM)**	**Predicate: Dimension® Ammonia Flex® reagent cartridge (AMON) k863840**
Intended Use	The AMM method is an *in vitro* diagnostic test for the quantitative measurement of ammonia in human plasma on the Dimension® clinical chemistry system. Ammonia measurements are used in the diagnosis and treatment of severe liver disorders such as cirrhosis, hepatitis and Reye's syndrome.	The AMON method used on the Dimension® clinical chemistry system is an *in vitro* diagnostic test intended for the quantitative determination of ammonia in human plasma.
Format	Prepackaged for use on an automated system	Prepackaged for use on an automated system
Measurement	Bichromatic Rate	Bichromatic Rate

Differences for Dimension® AMM assay:

Feature	**New Device: Dimension® Ammonia Flex® reagent cartridge (AMM)**	**Predicate: Dimension® Ammonia Flex® reagent cartridge (AMON) k863840**
Measuring Range	17-1277 µg/dL [10 – 750 µmol/L]	0 - 1000 µmol/L
Sample Size	44 µL	53 µL
Sample Type	Plasma (Lithium Heparin and EDTA)	Plasma (EDTA, Lithium Heparin, Sodium Fluoride)
Reagent Form	Liquid	Tablet

Note: Siemens has decided to offer our customers both conventional units and Systéme International d'Unités (SI units) in the Instructions for Use (IFU). The predicate, Dimension® Ammonia (AMON) assay results are reported in SI Units only. All data supplied in Appendix C will include both conventional units and SI Units for ease of review. Raw data was collected from the instruments in SI units and the conventional units were calculated using the following equation: µg/dL x 0.587 = [µmol/L].

11. Standard/Guidance Document Reference:

- Evaluation of Precision Performance of Quantitative Measurement in Methods; Approved Guideline (EP5-A2)
- Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline (EP6-A)
- Interference Testing in Clinical Chemistry; Approved Guideline (EP7-A2)
- Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (EP9-A2)
- Protocols for Determination of Limits of Detection and Quantitation; Approved Guideline (EP17-A)
- Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline (C28-A3)

12. Performance Characteristics

The following data represent typical performance for the Dimension® clinical chemistry system and were collected on a Dimension® RxL Max.

Method Comparison

Split sample comparison between the Dimension® Ammonia (AMM) assay and the Dimension® Ammonia (AMON) assay gave the following correlation statistics, when tested with patient samples:

Dimension® Ammonia (AMM) vs. Predicate

Dimension®	Predicate	Slope	Intercept µg/dL[µmol/L]	Correlation Coefficient (r)	n
AMM	Dimension® AMON	0.98	9 [5]	1.00	127

Plasma Comparison

To demonstrate equivalency between lithium heparin plasma and EDTA plasma for Dimension® AMM, comparison testing of 50 matched lithium heparin and EDTA plasma samples were tested on the Dimension® System and gave the following linear regression statistics:

Serum vs. Plasma Comparison Data

Lithium Heparin vs.	Slope	Intercept µg/dL[µmol/L]	Correlation Coefficient (r)	n
EDTA	0.96	1.6 [1.0]	1.00	50

Reference Interval (Expected Values)

The predicate Dimension® Ammonia (AMON) therapeutic range of 19 – 54 µg/dL [11 – 32 µmol/L] was validated for use with the Dimension® Ammonia (AMM) method by transference following CLSI C28-A3 *Defining, Establishing, and Verifying Reference Intervals in the Clinical Laboratory – Approved Guideline – Third Edition.* The Dimension® AMM assay is based on the same intended use and measuring principle as the predicate, Dimension® AMON. The literature reference used was the *Textbook of Clinical Chemistry* by NW Tietz; WB Saunders Co., Philadelphia, PA; pages 1487-1488.

Samples were collected from 30 healthy adults (17 men and 13 women) and analyzed with the Dimension® AMM method versus the predicate, Dimension® AMON method.

Expected Values: 11 – 32 µmol/L [19 - 54 µg/dL]

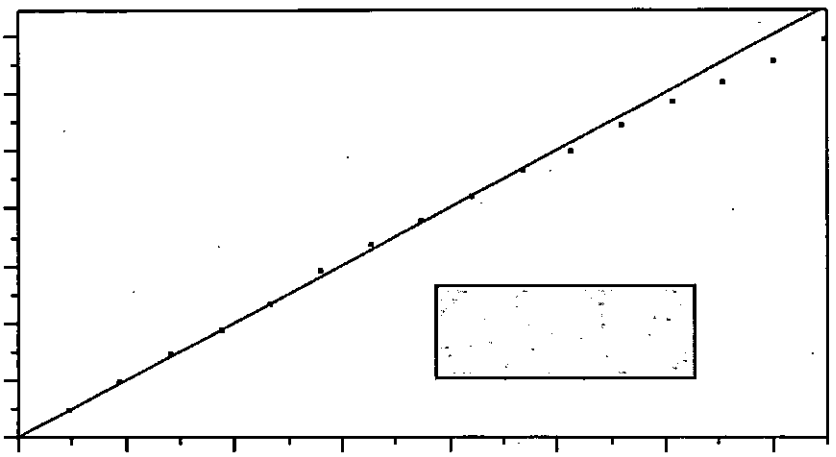
Precision

Precision testing was performed in accordance with CLSI EP5-A2 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline – Second Edition. Samples consisted of three levels of Liquichek™ Ethanol/Ammonia control. Testing was performed over 20 days, two separate runs with two test samples for each test material. Analysis of variance (ANOVA) was used to evaluate the data consistent with the recommendations of EP5-A2. The data are summarized in the following Dimension® Ammonia (AMM) Summary Table:

Material	Mean µg/dL	Mean [µmol/L]	Standard Deviation (%CV) Repeatability	Standard Deviation (%CV) Within-Lab
Liquichek™ Ethanol/Ammonia control				
Level 1	40	[23]	2.1 [1.2] (5.2)	3.7 [2.2] (9.3)
Level 2	187	[110]	2.6 [1.5] (1.4)	3.7 [2.2] (2.0)
Level 3	565	[332]	3.3 [1.9] (0.6)	7.3 [4.4] (1.3)

Linearity

The linear range was determined according to CLSI EP-6A, *Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline.* Based on the results of this testing and the Limit of Detection testing, the analytical measurement range was determined to be 17 – 1277 µg/dL [10 - 750 µmol/L].



Analytical Specificity/Interferences

The AMM method was evaluated for interference according to CLSI EP7-A2 Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition. Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference.

Substance Tested	Substance Concentration	Ammonia µg/dL [µmol/L]	Bias %
Hemoglobin (hemolysate)	75 mg/dL [0.05 mmol/L]	85 [50]	+11
	500 mg/dL [0.3105 mmol/L]	426 [250]	<10
Bilirubin (unconjugated)	60 mg/dL [1026 µmol/L]	85 [50]	<10
	80 mg/dL [1368 µmol/L]	426 [50]	<10
Bilirubin (conjugated)	80 mg/dL [1368 µmol/L]	85 [50]	<10
		426 [250]	<10
Lipemia (Intralipid®)	400 mg/dL [4.52 mmol/L]	85 [50]	*
		426 [250]	*
	200 mg/dL [2.26 mmol/L]	85 [50]	<10
		426 [250]	<10

*Lipemia (Intralipid®) at 400 mg/dL [4.52 mmol/L] and above tripped a test report message; interference could not be determined.

Studies were also performed following CLSI EP7-A2 for Interference Testing of exogenous substances at an ammonia concentration of 85 and 426 µg/dL and were found not to interfere with the AMM method when present in plasma. Inaccuracies (biases) were all less than 10%. See Dimension® AMM Instructions for Use for a full list of substances tested.

Interfering Substances

The AMM assay was evaluated for interference according to CLSI/NCCLS EP7-A2. Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference. Testing was performed at two levels of analyte concentration.

Analyte Test Level	**85 µg/dL [50 mmol/L]**		
Interferent	**[Test] mg/dL**	**[Test] SI Units**	**Bias (%)**
Albumin	6 g/dL	60 g/L	61
Bilirubin (unconjugated)	80mg/dL	136.8 µmol/L	-25
Dextran 40	500 mg/dL	125 µmol/L	20
Cholesterol	503 mg/dL	13 mmol/L	73
Creatinine	30 mg/dL	2.65 mmol/L	40
Hemoglobin	75 mg/dL	0.05 mmol/L (monomer)	11
Immunoglobulin G	5 g/dL	50 g/L	32
Uric Acid	20 mg/dL	1.2 mmol/L	56

Analyte Test Level	**426 µg/dL [250 mol/L]**		
Interferent	**[Test] mg/dL**	**[Test] S.I. Units**	**Bias (%)**
Albumin	6 g/dL	60 g/L	15
Dextran 40	3000 mg/dL	750 µmol/L	16
Cholesterol	503 mg/dL	13 mmol/L	34
Uric Acid	20 mg/dL	1.2 mmol/L	16

For certain endogenous interferents which exceeded 10 % bias, an aliquot of patient sample containing the potential interferent (test) was mixed with equal parts of a plasma pool containing approximately 85 µg/dL [50 µmol/L] ammonia (control). Test samples and control samples were processed and percent recovery calculated from expected and observed values. No significant interference was observed based on recovery within 10% of expected value.

Substance Tested	Test Concentration		AMM concentration	
	conventional	SI unit	µg/dL	[µmol/L]
Albumin	5.4 g/dL	54 g/L	170	[100]
Cholesterol	489 mg/dL	13 mmol/L	341	[200]
Creatinine	21.1 mg/dL	1.87 mmol/L	230	[135]
Triglyceride	1102 mg/dL	12.5 mmol/L	363	[213]
Uric Acid	9.3 mg/dL	0.6 mmol/L	145	[85]

Limit of Blank, Limit of Determination and Limit of Quantitation

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) was evaluated in accordance with CLSI EP17-A Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline. Studies were performed on the Dimension® clinical chemistry analyzer with the following results:

Dimension® Ammonia (AMM)		
Limit	**Protocol**	**Value**
LoB	4 samples of calibrator (zero level) were tested for 3 days, one run per day, 2 replicates per run, 2 reagent lots, 1 instrument	5 µg/dL [3 µmol/L]
LoD	4 low level samples were tested for 3 days, one run per day, 2 replicates per run, 2 reagent lots, 1 instrument	11 µg/dL [7 µmol/L]
LoQ	3 ammonia standards each diluted to 17 µg/dL [10 µmol/L] with purified water were tested for 3 days, one run per day, 3 replicates per run, 2 reagent lots, 1 instrument	17 µg/dL [10 µmol/L]

13. Conclusion: Based on the data presented, the Dimension® Ammonia (AMM) Flex® reagent cartridge is substantially equivalent in principle and performance to the Dimension® Ammonia (AMON) assay.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

February 15, 2013

Siemens Healthcare Diagnostics, Inc.
c/o Rose T. Marinelli
P.O. Box 6101/MS 514
Newark, DE 19714-6101

Re: k123320
Trade/Device Name: Dimension Ammonia Flex reagent cartridge (AMM)
Regulation Number: 21 CFR 862.1065
Regulation Name: Ammonia test system
Regulatory Class: I, reserved
Product Code: JIF
Dated: February 05, 2013
Received: February 07, 2013

Dear Ms. Marinelli:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please go to http://www.fda.gov/AboutFDA/CentersOffices/CDRH/CDRHOffices/ucm115809.htm for

the Center for Devices and Radiological Health's (CDRH's) Office of Compliance. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Carol C. Benson for

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k123320

Device Name: **Dimension® Ammonia Flex® reagent cartridge (AMM)**

Indications for Use:

The AMM method is an *in vitro* diagnostic test for the quantitative measurement of ammonia in human plasma (heparin or EDTA) on the Dimension® clinical chemistry system. Ammonia measurements are used in the diagnosis and treatment of severe liver disorders such as cirrhosis, hepatitis and Reye's syndrome

Prescription Use ___X___ And/Or Over the Counter Use ____.
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Denise Johnson-lyles -S
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Division Sign-Off
Office of In Vitro Diagnostics and Radiological Health

510(k) k123320